Linear Models of Aging: The Math

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1 The Gompertz equation

The Gompertz equations is the original equation used to model aging. It is represented by the simple form

$$\begin{aligned} \frac{dN}{dt} &= -\gamma(t)N(t) \\ \frac{d\gamma}{dt} &= a\gamma \end{aligned}$$

Now, the equation γ is a standard exponential growth, giving

$$\gamma = \gamma_0 e^{at}. \tag{1}$$

Plugging this into the equation for N gives

$$\frac{dN}{N} = -\gamma_0 e^{at} dt \tag{2}$$

solving for N gives

$$N = N_0 e^{\frac{-\gamma_0}{a}\left(e^{at}-1\right)}. \tag{3}$$

Surprisingly, such a simple equation does a good job of modeling death rates in adults while still having a simple closed form.

2 A Discreet Model

In our discreet model, we set up distinct cohorts that age, die, and give birth. They are represented by the following equations:

$$\begin{aligned} P_0(t+1) &= \alpha_1 P_1(t) + \alpha_2 P_2(t) + \cdots + \alpha_n P_n(t) \\ P_1(t+1) &= (1-\mu_0)P_0(t) \\ &\vdots \\ P_n(t+1) &= (1-\mu_{n-1})P_{n-1} \end{aligned}$$

These equations can be rewritten into the matrix form:

$$\mathbf{P}(t+1) = \mathbf{M}\mathbf{P}(t) \tag{4}$$

where $\mathbf{P}$ is a vector representing the number in each group and $\mathbf{M}$ is a matrix of conversion coefficients. Within $\mathbf{M}$, the top row is the birth rate α for each class, and just below the diagonal is the survival rate $1-\mu$ for each group.

Now, we know that the population matrix is non negative. Additionally, this matrix is primitive, meaning that the matrix becomes positive when exponentiated. Thus, the Perron-Frobenius theorem says that if A is non-negative and primitive, there is some dominant eigenvalue, greater than 0, that is also greater than any other eigenvalue. Thus, the population will approach some steady state distribution with a well defined growth ratio - the dominant eigenvalue.

3 A Continuous Model

Here, we use differential equations to represent transitions from one discreet group to another. In our simple model, we assume each group decays exponentially.

$$\begin{aligned}
\frac{dS_0}{dt} &= -S_0 \\
\frac{dS_1}{dt} &= S_0 - S_1 \\
&\vdots \\
\frac{dS_j}{dt} &= S_j - S_{j-1} \\
&\vdots
\end{aligned}$$

Now,

$$\begin{aligned}
\frac{d}{dt}(S) &= \frac{d}{dt}(-S + (S_0 - S_1) + (S_1 - S_2) + \cdots \\
&= 0
\end{aligned}$$

so long as we ignore any effect from having a last grouping. Thus, in this model, with no birth or death, we simply have an aging of the population.

4 A Continuous Model with Birth

Here, we model tracking the number of stem cells in a population. Every cell has some chance of self-replicating (p) and some chance of producing a differentiated cell (f). The

age representees the total number of times a cell has divided. We have the differential equations:

$$\begin{aligned}
\frac{dS_0}{dt} &= -(p+f)S_0 \\
&\vdots \\
\frac{dS_j}{dt} &= (2p+f)S_{j-1} - (p+f)S_j \\
&\vdots
\end{aligned}$$

Now,

$$\begin{aligned}
\frac{dS}{dt} &= \frac{d}{dt}\sum_j S_j \\
&= -(p+f)S_0 + (2p+f)S_0 - (p+f)S_1 + \cdots \\
&= ps
\end{aligned}$$

if one assumes that there is no final group. Thus, the total number of cells grows exponentially.

Now, the cells have a telomere length $\bar{L}$ that shortens by an average of 100 base pairs as the cell divides. We can write

$$\begin{aligned}
\bar{L}(t) &= \frac{1}{S(t)}\sum (L_0 - 100j)S_j(t) \\
&= L_0 - 100\frac{L(t)}{S(t)}
\end{aligned}$$

where L_0 represents the initial average telomere length and $L(t) = \sum jS_j(t)$.

Now,

$$\begin{aligned}
\frac{d(jS_j)}{dt} &= (2p+f)(jS_{j-1}) - (p+f)(jS_j) \\
\frac{dL}{dt} &= (2p+f)\sum[(j-1)S_{j-1} + S_{j-1}] - (p+f)\sum jS_j \\
&= (2P+f)L + (2p+f)s - (p+f)L \\
&= pL + (2p+f)S
\end{aligned}$$

where we have once again assumed no affect from a final group. We can not calculate a change in the average telomere length:

$$\frac{d\bar{L}}{dt} = -100\frac{d\frac{L(t)}{S(t)}}{dt}$$

$$
\begin{aligned}
&= -100(S(t)\frac{dL}{dt} - L(t)\frac{dS}{dt} \\
&= \frac{-100}{S^2}[S(pl + (2p + f)S) - PSL] \\
&= -100(2p + f).
\end{aligned}
$$

Now, we can determine p from the growth rate of the cells. We can find the change in the rate of telomere by looking at cells. Therefore, we can find f, the rate of differentiation.

5 Conclusion

Despite the simplicity of these aging models, a lot of useful predictions about cell behavior can be made. These models, then, provide a useful starting place for modeling aging, with added complexity added where needed for a given application. Moreover, this process shows the importance of starting from the basics and adding on features. This allows for a simplicity in interpreting the model but also ensures that the behavior at every stage is reasonable.